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## **Jardiance® (empagliflozin) significantly reduced the risk of progressive kidney disease in adults with type 2 diabetes with established cardiovascular disease**

**-- JARDIANCE is the only SGLT2 inhibitor to demonstrate the potential to improve kidney outcomes on top of standard of care**

**-- New data from the landmark EMPA-REG OUTCOME® clinical trial published in *The New England Journal of Medicine***

RIDGEFIELD, Conn. and INDIANAPOLIS, June 14, 2016 /PRNewswire/ -- New data showed Jardiance® (empagliflozin) reduced the risk for new-onset or worsening kidney disease by 39 percent versus placebo when added to standard of care in adults with type 2 diabetes with established cardiovascular disease. Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) announced today that the findings have been published in *The New England Journal of Medicine* and also presented at the American Diabetes Association (ADA) 76th Scientific Sessions® in New Orleans.

"These findings are clinically important, given that more than a third of people with type 2 diabetes will develop kidney disease, which can lead to kidney failure and eventually the need for dialysis. In the United States, the cost to treat chronic kidney disease is estimated to exceed \$48 billion annually," said Christoph Wanner, M.D., chief of the Division of Nephrology and Hypertension at the University Hospital of Würzburg, Germany. "Since diabetes is the number one cause of kidney failure in the U.S., novel treatments that may have the potential to help address this crucial medical need are necessary."

These findings were part of a pre-specified exploratory analysis plan of additional endpoints of the landmark EMPA-REG OUTCOME® trial. New-onset or worsening kidney disease was a pre-specified composite endpoint that included the below clinical events. Compared with placebo, JARDIANCE led to the following statistically significant changes in outcomes:

- | 55 percent reduction in the initiation of renal replacement therapy (such as dialysis)
- | 44 percent reduction in doubling of creatinine (a waste product usually filtered by the kidneys) in the blood
- | 38 percent reduction in progression to macroalbuminuria (very high levels of a protein called albumin in the urine)

JARDIANCE also significantly slowed the decline in kidney function over time compared with placebo. Most patients in this trial were already taking the recommended standard treatment for kidney disease in type 2 diabetes, renin angiotensin aldosterone system blockade; the renal effects of JARDIANCE were apparent on top of these agents.

Consistent risk reductions in kidney outcomes with JARDIANCE were seen in adults who had impaired kidney function, or increased levels of albumin in the urine, at baseline and in those who did not, according to a post hoc sub-group analysis. Serious adverse events (AEs) and AEs leading to treatment discontinuation for JARDIANCE versus placebo were comparable for those with or without impaired kidney function at baseline. Death due to renal disease was rare and occurred in three patients treated with JARDIANCE (0.1 percent) and none treated with placebo.

"With these new EMPA-REG OUTCOME data, JARDIANCE is the only SGLT2 inhibitor associated with evidence of slowing the progression of kidney disease in adults with type 2 diabetes and established cardiovascular disease in a cardiovascular outcome study," said Professor Hans-Juergen Woerle, global vice president medicine, Boehringer Ingelheim.

### **About the EMPA-REG OUTCOME Trial (NCT01131676)**

EMPA-REG OUTCOME was a long-term, multicenter, randomized, double-blind, placebo-controlled trial of more than 7,000 patients from 42 countries with type 2 diabetes and established cardiovascular (CV) disease.

The study assessed the effect of JARDIANCE (10 mg or 25 mg once daily) added to standard of care compared with placebo added to standard of care. Standard of care was comprised of glucose-lowering agents and CV drugs (including for blood pressure and cholesterol). The primary endpoint was defined as time to first occurrence of CV death, non-fatal heart attack or non-fatal stroke.

Over a median of 3.1 years, JARDIANCE significantly reduced the risk of CV death, non-fatal heart attack or non-fatal stroke

by 14 percent versus placebo. Risk of CV death was reduced by 38 percent, with no significant difference in the risk of non-fatal heart attack or non-fatal stroke.

The overall safety profile of JARDIANCE in the EMPA-REG OUTCOME trial was consistent with that of previous trials.

### **About Diabetes and Cardiovascular Disease**

Approximately 29 million Americans and an estimated 415 million people worldwide have diabetes, and nearly 28 percent of Americans with diabetes—totaling 8 million people—are undiagnosed. In the U.S., approximately 12 percent of those aged 20 and older have diabetes. Type 2 diabetes (T2D) is the most common type, accounting for an estimated 90 to 95 percent of all diagnosed adult diabetes cases in the U.S. Diabetes is a chronic condition that occurs when the body either does not properly produce, or use, the hormone insulin.

Due to the complications associated with diabetes, such as high blood sugar, high blood pressure and obesity, cardiovascular (CV) disease is a major complication and the leading cause of death associated with diabetes. People with diabetes are two to four times more likely to develop CV disease than people without diabetes. In 2015, diabetes caused 5 million deaths worldwide, with CV disease as the leading cause. Approximately 50 percent of deaths in people with T2D worldwide are caused by CV disease. In the U.S., health care costs for managing cardiovascular conditions in patients with diabetes totalled more than \$23 billion dollars in 2012.

### **About Diabetes and Kidney Disease**

Kidney disease develops in approximately 35 percent of patients with type 2 diabetes (T2D) and is associated with increased risk of death. Long-term kidney problems, known as chronic kidney disease, can lead to kidney failure in its final stages and typically necessitates either dialysis or a kidney transplant. Nearly 44 percent of new cases of kidney failure are due to diabetes, and up to 40 percent of people with T2D in the U.S. will eventually suffer from kidney failure.

### **What is JARDIANCE?**

JARDIANCE is a prescription medicine used along with diet and exercise to lower blood sugar in adults with type 2 diabetes. JARDIANCE is not for people with type 1 diabetes or for people with diabetic ketoacidosis (increased ketones in the blood or urine).

## **IMPORTANT SAFETY INFORMATION**

### **What is the most important information I should know about JARDIANCE?**

#### **JARDIANCE can cause serious side effects, including:**

- ▮ **Dehydration.** JARDIANCE can cause some people to have dehydration (the loss of body water and salt). Dehydration may cause you to feel dizzy, faint, light-headed, or weak, especially when you stand up.  
  
You may be at a higher risk of dehydration if you:
  - ▮ have low blood pressure
  - ▮ take medicines to lower your blood pressure, including water pills (diuretics)
  - ▮ are on a low salt diet
  - ▮ have kidney problems
  - ▮ are 65 years of age or older.
- ▮ **Ketoacidosis (increased ketones in your blood or urine).** Ketoacidosis can be life threatening and may need to be treated in the hospital. Ketoacidosis occurs in people with type 1 diabetes and can also occur in people with type 2 diabetes taking JARDIANCE, even if blood sugar is less than 250 mg/dL. **Stop taking JARDIANCE and call your doctor right away if you get any of the following symptoms**, and if possible, check for ketones in your urine:
  - ▮ nausea
  - ▮ vomiting
  - ▮ stomach-area (abdominal) pain
  - ▮ tiredness
  - ▮ trouble breathing
- ▮ **Serious urinary tract infections.** Serious urinary tract infections can occur in people taking JARDIANCE and may lead to hospitalization. Tell your doctor if you have symptoms of a urinary tract infection such as a burning feeling when passing urine, a need to urinate often or right away, pain in the lower part of your stomach or pelvis, or blood in the urine. Sometimes people also may have a fever, back pain, nausea or vomiting.
- ▮ **Vaginal yeast infection.** Women who take JARDIANCE may get vaginal yeast infections. Talk to your doctor if you experience vaginal odor, white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese),

and/or vaginal itching.

- | **Yeast infection of the penis.** Men who take JARDIANCE may get a yeast infection of the skin around the penis, especially uncircumcised males and those with chronic infections. Talk to your doctor if you experience redness, itching or swelling of the penis, rash of the penis, foul smelling discharge from the penis, and /or pain in the skin around penis.

### **Who should not take JARDIANCE?**

**Do not take** JARDIANCE if you are allergic to empagliflozin or any of the ingredients in JARDIANCE. Symptoms of serious allergic reactions to JARDIANCE may include:

- | skin rash
- | raised red patches on your skin (hives)
- | swelling of the face, lips, tongue, and throat that may cause difficulty breathing or swallowing.

If you have any of these symptoms, stop taking JARDIANCE and contact your doctor or go to the nearest emergency room right away.

**Do not take** JARDIANCE if you have severe kidney problems or are on dialysis.

### **What should I tell my doctor before using JARDIANCE?**

#### **Tell your doctor if you:**

- | have kidney problems. Your doctor may do blood tests to check your kidneys before and during your treatment with JARDIANCE
- | have liver problems
- | have a history of urinary tract infections or problems with urination
- | are going to have surgery
- | are eating less due to illness, surgery, or a change in your diet
- | have or have had problems with your pancreas, including pancreatitis or surgery on your pancreas
- | drink alcohol very often, or drink a lot of alcohol in the short term ("binge" drinking)
- | have any other medical conditions
- | are pregnant or planning to become pregnant. It is unknown if JARDIANCE will harm your unborn baby
- | are breastfeeding, or plan to breastfeed. It is unknown if JARDIANCE passes into your breast milk.

**Tell your doctor about all the medicines you take** including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially tell your doctor if you take water pills (diuretics) or medicines that can lower your blood sugar such as insulin.

### **What are other possible side effects of JARDIANCE?**

- | **Low blood sugar** (hypoglycemia): if you take JARDIANCE with another medicine that can cause low blood sugar, such as sulfonylurea or insulin, your risk of low blood sugar is higher. The dose of your sulfonylurea or insulin may need to be lowered. Symptoms of low blood sugar may include:
  - | Headache
  - | Drowsiness
  - | Weakness
  - | Dizziness
  - | Confusion
  - | Irritability
  - | Hunger
  - | Fast heart beat
  - | Sweating
  - | Shaking or feeling jittery
- | **Kidney Problems**, especially in people 75 years of age or older and people who already have kidney problems
- | **Increased fats in your blood (cholesterol).**

**The most common side effects of JARDIANCE** include urinary tract infections, and yeast infections in females.

**You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.**

For more information, please see [full Prescribing Information, including Patient Information](#).

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### **Boehringer Ingelheim and Eli Lilly and Company**

In January 2011, Boehringer Ingelheim and Eli Lilly and Company announced an alliance in diabetes that centers on compounds representing several of the largest diabetes treatment classes. This alliance leverages the strengths of two of the world's leading pharmaceutical companies. By joining forces, the companies demonstrate commitment in the care of patients with diabetes and stand together to focus on patient needs. Find out more about the alliance at [www.boehringer-ingelheim.com](http://www.boehringer-ingelheim.com) or [www.lilly.com](http://www.lilly.com).

### **About Boehringer Ingelheim Pharmaceuticals, Inc.**

Boehringer Ingelheim Pharmaceuticals, Inc., based in Ridgefield, CT, is the largest U.S. subsidiary of Boehringer Ingelheim Corporation.

Boehringer Ingelheim is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, the company operates globally with 145 affiliates and more than 47,000 employees. Since its founding in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel treatments for human and veterinary medicine.

Boehringer Ingelheim is committed to improving lives and providing valuable services and support to patients and families. Our employees create and engage in programs that strengthen our communities. To learn more about how we make more health for more people, visit our [Corporate Social Responsibility Report](#).

In 2015, Boehringer Ingelheim achieved net sales of about \$15.8 billion dollars (14.8 billion euros). R&D expenditure corresponds to 20.3 percent of its net sales.

For more information please visit [www.us.boehringer-ingelheim.com](http://www.us.boehringer-ingelheim.com), or follow us on Twitter @BoehringerUS.

### **About Lilly Diabetes**

Lilly has been a global leader in diabetes care since 1923, when we introduced the world's first commercial insulin. Today we are building upon this heritage by working to meet the diverse needs of people with diabetes and those who care for them. Through research and collaboration, a broad and growing product portfolio and a continued determination to provide real solutions—from medicines to support programs and more—we strive to make life better for all those affected by diabetes around the world. For more information, visit [www.lillydiabetes.com](http://www.lillydiabetes.com) or follow @LillyDiabetes.

### **About Eli Lilly and Company**

Lilly is a global healthcare leader that unites caring with discovery to make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at [www.lilly.com](http://www.lilly.com) and [newsroom.lilly.com/social-channels](http://newsroom.lilly.com/social-channels).

*This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about JARDIANCE as a treatment for patients with type 2 diabetes along with diet and exercise and reflects Lilly's current belief. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with the results to date or that JARDIANCE will receive additional regulatory approvals. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.*

Jardiance® is a registered trademark of Boehringer Ingelheim

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**CONTACT:**

**Jennifer Forsyth**

Director, Public Relations

Boehringer Ingelheim Pharmaceuticals, Inc.

Email: [jennifer.forsyth@boehringer-ingelheim.com](mailto:jennifer.forsyth@boehringer-ingelheim.com)

Phone: (203) 791-5889

**Molly McCully**

Communications Manager

Lilly Diabetes

Email: [mccully\\_molly@lilly.com](mailto:mccully_molly@lilly.com)

Phone: (317) 478-5423



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